

Applicants: Nathan Ellis, James German, and Joanna Groden
Serial No.: 09/753,143
Filed: January 2, 2001
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Amendments to the Specification:

Please amend the previously amended paragraph on page 13, line 28, through page 14, line 16 as follows. Note that the underlining of "supra" and of the Journal titles appear in the original text.

The persons with BS in whom low-SCE lymphocytes have arisen were described previously. Epstein-Barr virus transformed lymphoblastoid cell lines (LCLs) were developed from these and other persons with BS by standard culture methods using material obtained through the Bloom's Syndrome Registry (German and Passarge, supra). The recombinant low-SCE LCLs in which reduction to homozygosity had been detected, and the cells used to determine the constitutional genotypes of the five persons from whom these recombinant low-SCE LCLs were developed, also have been described. The polymorphic loci typed included some previously reported (Beckmann, J. S., et al. Hum. Mol. Genet. 2:2019-2030 (1993); Gyappay Gyapay, G., et al. Nature Genetics 7:246-339 (1994)) and others that were identified during the physical mapping of the BLM region of chromosome 15. The methods of preparation of DNA samples, oligonucleotide primers, and conditions for PCR amplification of microsatellite polymorphisms on chromosome 15 have been described (German, et al., 1994, supra; Ellis, N. A., et al. Am. J. Hum. Genet. 55:453-460 (1994)).

Please amend the previously amended paragraph on page 19, line 23, through page 20, line 8, as follows. Note that the underlining of "supra" appear in the original text.

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BLM previously was localized by SCP mapping to a 1.3 cM interval bounded proximally by *D15S116* and distally by four tightly linked loci *D15S127*, *FES*, *D15S158*, and *IP15M9*. The four loci are present in a 1-2 cM interval on chromosome 15 (Beckmann, et al., *supra*; Gyappay Gyapay, et al., *supra*). The order of these four loci was determined by PCR analysis of clones in a 2-Mb YAC and P1 contig that encompasses *BLM*. The four loci were oriented with respect to the telomere by finding a recombinant chromosome in a BS family in which crossing-over had occurred between *BLM* and *IP15M9*, placing *IP15M9* on the distal end of the contig (Fig. 1A). Because *D15S127* was the most proximal locus that was reduced to homozygosity in low-SCE LCLs, polymorphic loci in the region proximal to it were sought. There, a polymorphic locus, *D15S1108*, was identified that remained constitutionally heterozygous in the recombinant low-SCE LCLs, in contrast to locus *D15S127* that had become homozygous in them (Fig. 1B). This shift from heterozygosity to homozygosity of markers indicated that *BLM* is situated in the 250-kb region between *D15S1108* and *D15S127*.

On page 34-35, please replace Table 1 with the substitute Table 1 attached hereto as **Exhibit 1**. No amendments have been made to the version of Table 1 attached in Exhibit 1. Rather, the substitute Table is attached to provide a clearer and more legible version of the Table than is apparently available to the Examiner.

On page 35, please amend the paragraph on lines 2-3 as follows.

⁸ The insertion substitution of an A bp for a G bp causes the insertion of a novel codon for K after amino acid 514 position (taken from the H1-5' sequence, Fig. 2), and after this codon there is a stop codon.